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Re-evaluation Note REV2016-13

Special Review of Carbaryl: Proposed Decision for Consultation

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1.0 Introduction

Pursuant to subsection 17(2) of the *Pest Control Products Act*, Health Canada's Pest Management Regulatory Agency (PMRA) initiated a special review of pest control products containing carbaryl, based on the 2007 European Commission regulatory decision. The initiation of the special review of carbaryl was announced in December 2013 (Canada, 2013).

Pursuant to subsection 18(4) of the *Pest Control Products Act*, the PMRA has evaluated the aspects of concern that prompted the special review of carbaryl. The aspects of concern are relevant to human health (toxicity of metabolites and potential carcinogenicity of carbaryl) and the environment (potential risk to non-target organisms).

2.0 Uses of Carbaryl in Canada

Carbaryl is registered for the control of a broad range of insect pests. It is also registered for use as a plant growth regulator for apple thinning. There are currently two technical grade active ingredients, one manufacturing concentrate as well as 11 commercial class and 19 domestic class end-use products registered in Canada. All registered pest control products containing carbaryl are considered in this special review (Appendix I).

The PMRA completed the re-evaluation of carbaryl in 2016. As a result of the re-evaluation, all domestic class products, all turf applications (lawns, sod farms and golf courses), a number of agricultural uses (for example, alfalfa, barley, wheat, cherries, grapes, corn, strawberries) and the commercial application of carbaryl in residential settings were cancelled (Canada, 2016). For the remaining uses, several risk reduction measures were implemented (such as additional personal protective equipment for mixers/loaders/applicators, restricted-entry intervals for postapplication workers, changes to application timing, restriction of application during blooming for some crops, and buffer zones to protect the environment).

3.0 Aspects of Concern that Prompted the Special Review

The concerns identified in the 2007 European Commission Decision to prohibit all uses of carbaryl (European Commission, 2006; 2007) were considered for this special review, and were related to:

- Human Health
  - Toxicity of metabolites: 4-hydroxycarbaryl and 5-hydroxycarbaryl
  - Potential carcinogenicity of carbaryl

- Environment
  - Potential risk to beneficial arthropods
  - Potential chronic risk to birds
  - Potential acute risk to mammals
  - Potential acute and chronic risk to aquatic organisms

4.0 PMRA Evaluation of the Aspects of Concern for Carbaryl that Prompted the Special Review

Following the initiation of the special review, the PMRA requested information related to the aspects of concern from provinces and other relevant federal government departments and agencies in accordance with the subsection 18(2) of the *Pest Control Products Act*.

In order to evaluate the aspects of concern for carbaryl, the PMRA has considered currently available relevant scientific information, including information from the re-evaluation of carbaryl in Canada (Canada, 2009; 2016), from the European Union, such as the 2006 European Food Safety Authority report (European Commission, 2006), from the Joint Meeting on Pesticide Residues (JMPR) (JMPR, 1970), and any relevant information obtained since then (for example, information from the Canadian incident report database, and water monitoring data).

4.1 Toxicity of Metabolites: 4-hydroxycarbaryl and 5-hydroxycarbaryl

The PMRA considered the toxicity study of the plant metabolites 4-hydroxycarbaryl and 5-hydroxycarbaryl (JMPR, 1970). Data from the in vitro assay in bovine erythrocytes suggested that both metabolites can inhibit cholinesterase activity. In an acute oral toxicity study in rats, 4-hydroxycarbaryl was less toxic (lethal does 50% [LD_{50}] of 1190 mg/kg bodyweight [bw]) than carbaryl (LD_{50} range from 200 to 850 mg/kg bw) (Canada, 2009; JMPR, 1970), whereas 5-hydroxycarbaryl was of similar toxicity (LD_{50} of 297 mg/kg bw). The PMRA also considered a short-term dietary study in rats with the two metabolites. No effects were observed with 4-hydroxycarbaryl or 5-hydroxycarbaryl at the highest dose tested (1000 mg/kg bw/day), while carbaryl showed inhibition of erythrocyte cholinesterase and decreased bodyweight at 250 mg/kg bw/day, thus confirming that 4-hydroxycarbaryl and 5-hydroxycarbaryl were not more toxic than carbaryl.

The PMRA assessment also considered carbaryl metabolism studies conducted on three different crops: radish, lettuce, and soybean (Canada, 2009). It was concluded that the nature of the residues of carbaryl in plants is adequately understood. The metabolites 4-hydroxycarbaryl and 5-hydroxycarbaryl were identified as minor residues, with less than or equal to 2.7% of the total radioactive residue. Surface residues on radish tops, lettuce, and soybean forage accounted for 38-67% of the total radioactive residue, and these residues were primarily unconjugated carbaryl. Various other conjugated and unconjugated residues were found and they include N-(hydroxymethyl) carbaryl (N-OH-Me carbaryl), 1- naphthol and 5,6-dihydro-dihydroxy-1-naphthol, malonylglycoside conjugate of 1-naphthol, and a hexose conjugate of N-OH-Me carbaryl.

Since 4-hydroxycarbaryl and 5-hydroxycarbaryl are minor residues (<10% of the total radioactive residue) and are less toxic than carbaryl, they are not included as residues of concern in plants (Canada, 2009). In turn, the PMRA considered the parent compound as the only residue of concern in plants, and conducted acute and chronic dietary exposure assessments considering all registered and imported commodities, including apple. The review concluded that acute dietary exposure to carbaryl was not of concern for all Canadian population groups.

Acute dietary exposure (from food) estimates were 29% (general population) and 54% (children 1-2 years of age) of the acute reference dose. The chronic dietary exposure estimates (from food) represented less than 2% of the acceptable daily intake for all sub-populations, and therefore, there is no risk of concern (Canada, 2009).

4.2 Potential Carcinogenicity of Carbaryl

As part of the assessment, the PMRA considered the chronic dietary feeding studies in rats and mice (Canada, 2009). In rats, at the high dose, tumors included bladder tumors in both sexes (transitional cell papillomas and carcinomas) and hepatic adenomas in females. The high doses exceeded maximum tolerated doses and thus, are considered inappropriate for carcinogenicity testing. In mice, the tumors observed at the high dose included renal tubular cell tumors in males (combined adenomas/carcinomas), liver tumors in females (combined adenomas/carcinoma) and combined vascular tumors in both sexes. The mouse study also showed increased incidences of vascular tumors (hemangiomas and hemangiosarcomas mostly in the liver and spleen) at low and mid dose in males (8% and 13%, respectively, compared to 3% in controls). The observed increases were statistically significant starting at the mid dose level ($\leq$0.05). Although historical data in mice were not available from the performing laboratory for a 24-month duration, hemangiosarcomas were the cause of death in a number of animals in the study. A quantitative cancer risk assessment was conducted on the vascular tumors noted in the long-term mouse study. The unit risk (q_1*) is 1.08×10^{-3} $(mg/kg\ bw/day)^{-1}$ based on vascular tumors (combined hemangioma and hemangiosarcoma) in male mice.

Based on the q_1* approach, the PMRA conducted a cancer risk assessment and it indicated that the lifetime cancer risk estimate from dietary exposure is 7×10^{-8} for the general population, which is below the threshold of 1×10^{-6}, indicating no risk of concern (Canada, 2009). In addition, the PMRA conducted a cancer risk assessment for occupational mixers, loaders and applicators, postapplication workers and bystanders. The calculated cancer risks are below the threshold (Canada, 2016), and therefore, are not of concern.

While no cancer risks of concern were identified as part of this assessment, as mentioned in section 2.0, the PMRA has implemented several risk reduction measures to minimize potential non-cancer risks from carbaryl (Canada, 2016). The risk reduction measures include the cancellation of products and uses (such as domestic class products, turf use, and a number of agricultural uses), additional personal protective equipment and engineering control requirements, re-entry intervals as well as revised application rates, frequencies and intervals.

4.3 Potential Risk to Beneficial Arthropods

Beneficial arthropods could be exposed to carbaryl through spray drift or by consumption of sprayed crops. Data from acute toxicity study indicated that carbaryl is highly toxic to honey bees (oral and contact LD_{50} were 0.11-0.14 and 1.1-1.3 µg a.i./bee, respectively). The in-field risk quotient (RQ) ranged from 1.3 to 20.2 depending on the application rates, indicating a risk of concern.

Therefore, the PMRA implemented several risk reduction measures to minimize the exposure, including changes to application timing and restriction of application during bloom for some crops (Canada, 2016).

4.4 Potential Chronic Risk to Birds

Birds could be exposed to carbaryl through spray drift or by consumption of sprayed vegetation or contaminated prey. A screening-level risk assessment was initially performed using the estimated environmental concentrations (EECs) for a direct overspray scenario. The EECs were converted to estimated daily exposure for each body weight considering food ingestion rate and body weight. When the screening level assessment results in a potential risk (RQ >1), then a refined assessment is conducted with more realistic exposure scenarios (for example, drift to non-target habitats).

The PMRA considered chronic studies conducted with mallard duck (NOEC of 300 mg a.i./kg diet) and northern bobwhite (dietary LC_{50} was > 5000 mg/kg diet). Based on these endpoints, the screening level risk assessment indicated a potential chronic risk of concern to birds. Following a refined assessment, the chronic RQ values were < 1.4, indicating a potential chronic risk for birds from off-field contaminated food sources at the higher application rate (uses on turf). The use on turf has been cancelled (Canada, 2016) and chronic RQ values for the remaining use pattern are below the level of concern (RQ < 1). Despite the fact that chronic RQ values are < 1 with the remaining use pattern, the PMRA has included environmental hazard statements to inform users of potential risks to birds (Canada, 2016).

4.5 Potential Acute Risk to Mammals

Mammals could be exposed to carbaryl through spray drift or by consumption of sprayed vegetation or contaminated prey. Acute toxicity studies in mammals showed that oral LD_{50} were 175-600 mg a.i./kg bw in mouse, and 200-850 mg a.i./kg bw in rat. A screening level risk assessment indicated a potential acute risk of concern to mammals. The refined acute RQ values ranged from 1.3 to 20, indicating a potential acute risk for mammals from off-field contaminated food sources. Therefore, the PMRA has included environmental hazard statements for mammals to inform users of the potential risks to mammals (Canada, 2016). The cancellation of certain uses and certain products containing carbaryl (Canada, 2016) further reduces potential risk to mammals.

4.6 Potential Risk to Aquatic Organisms

Aquatic organisms can be exposed to carbaryl as a result of spray drift and run-off. The PMRA reviewed aquatic ecotoxicity studies for carbaryl to assess the potential risk to aquatic organisms. Based on available information, an LC_{50} of 10 µg a.i./L for freshwater inveterbrate (based on mesocosm study) and ½ LC_{50} of 3.1 µg a.i./L for marine invertebrate were considered as the most appropriate endpoints for the aquatic risk assessment (Canada, 2016).

The PMRA assessed risks to aquatic organisms from spray drift and surface water run-off. The potential risk from spray drift was based on estimated environmental concentration (EECs) in water from groundboom application and the expected deposition from spray drift of 11% at 1 m downwind from the point of application. RQ values for aquatic organisms ranged from 30 to 160, indicating a potential risk to aquatic organisms from spray drift. A refined assessment for run-off was conducted using EECs based on modelling and monitoring data. Based on modelling (using conservative assumptions), risks of concern were identified for aquatic organisms. Based on the surface water monitoring information, risk to aquatic organisms slightly exceeded the level of concern (RQs ranged from 1.1 to 3.5).

Consequently, to reduce the risks to aquatic organisms, the PMRA implemented several risk reduction measures, including the requirement for buffer zones, precautionary statements and other best practices (for example, instructions to avoid application to areas with a moderate slope and when heavy rain is forecast, inclusion of vegetative strip between the treated area and the edge of the water body) (Canada, 2016). The cancellation of certain uses and certain products containing carbaryl (Canada, 2016) further reduces the potential risk to aquatic organisms.

5.0 Incident reports

Since 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the PMRA website.

As of 11 February 2016, the PMRA has received six incident reports related to the aspects of concern. There was one major environment incident in which fish were killed when water that was used to extinguish a chemical warehouse fire was released into a nearby stream. The remaining environment incidents were minor (four incidents) to moderate (one incident) in severity and involved honeybees; however, other chemical active ingredients in addition to carbaryl were also reported in these incident reports. The recently implemented pollinator statements further reduces the occurrence of future incidents involving carbaryl.

6.0 Proposed Special Review Decision for Carbaryl

Evaluation of available relevant scientific information related to the aspects of concern indicates that potential risks to health and environment from products containing carbaryl are acceptable, taking into account the current risk reduction measures implemented in 2016 (Canada, 2016). On this basis, Health Canada's Pest Management Regulatory Agency, under the authority of the *Pest Control Products Act*, is proposing to confirm the current registration of carbaryl products for sale and use in Canada pursuant to subsection 21(1) of the *Pest Control Product Act*.

This proposed special review decision is a consultation document.[1] The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

[1] "Consultation statement" as required by Subsection 28(2) of the Pest Control Products Act.

7.0 Next Steps

Before making a special review decision on carbaryl, the PMRA will consider all comments received from the public in response to this consultation document. A science-based approach will be applied in making a final decision on carbaryl. The PMRA will then publish a special review decision document, which will include the decision, the reasons for it, a summary of the comments received on the proposed decision and the PMRA's response to these comments.

Appendix I Registered Products Containing Carbaryl as of 13 July 2016

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
18463	Technical	Tessenderlo Kerley, Inc	Sevin Brand Technical Carbaryl Insecticide	SO	99.5%
30614	Technical	Bayer CropScience Inc	Sevin Brand Carbaryl Technical	SO	99.5%
19351	Manufacturing concentrate	Bayer CropScience Inc	Sevin Brand 97.5% Manufacturing Concentrate	SO	97.5%
16653	Commercial + Restricted uses	Bayer CropScience Inc	Sevin T&O Insecticide	SU	43%
27876	Commercial + Restricted uses	Tessenderlo Kerley, Inc	Sevin XLR Carbaryl Insecticide Liquid Suspension	SU	42.8%
9042	Commercial	Dominion Veterinary Laboratories Ltd	Sevin Dispersible Powder Insecticide (For Veterinary Use Only)	DU	50%
9061	Commercial	Dominion Veterinary Laboratories Ltd	Dominion Dusting Powder For (Veterinary Use Only)	DU	5%
17534	Commercial	Agrium Advanced Technologies RP Inc	Farm & Ranch Brand Sevin 5-D Insecticide Dust	DU	5%
22339	Commercial	Bayer CropScience Inc	Chipco Sevin RP2 Carbaryl Insecticide Liquid Suspension	SU	22.5%
25815	Commercial	Peacock Industries	Eco Bran Grasshopper Insecticide Agricultural	GR	2%
26873	Commercial	Bayer CropScience Inc	Chipco Sevin T&O Carbaryl Insecticide	SU	42.8%
9986	Domestic	King Home and Garden Inc.	King Fruit Tree And Garden Spray	DU	10%[1]
10565	Domestic	Sure-Gro IP Inc.	Wilson Rose Doctor Insecticide-Fungicide	DU	5%[1]
12135	Domestic	Sure-Gro IP Inc.	Wilson Sevin Garden Dust Insecticide	DU	5%
14851	Domestic	King Home & Garden Inc.	Gardal Rose, Flower, & Evergreen Dust	DU	5%[1]
14852	Domestic	Sure-Gro IP Inc.	Wilson Bulb & Soil Dust	DU	5%[1]
17424	Domestic	Sure-Gro IP Inc.	Wilson Garden Doctor Insecticide-Fungicide	DU	5%[1]
17971	Domestic	Sure-Gro IP Inc.	Wilson Liquid Sevin Carbaryl Insecticide	SU	22.5%
19228	Domestic	Sure-Gro IP Inc.	Wilson Earwig & Cutworm Destroyer	GR	5%
25870	Domestic	Bayer CropScience Inc.	Sevin RP2 Domestic Carbaryl Insecticide Liquid Suspension	SU	22.5%
26698	Domestic	Sure-Gro IP Inc.	Wilson Sevin Grubout Ant & Grub Killer Concentrate	EC	22.5%
26699	Domestic	Sure-Gro IP Inc.	Wilson Sevin Grubout Ant & Grub Killer	EC	22.5%
26702	Domestic	Sure-Gro IP Inc.	Wilson Antout Ant Killer Attach And Spray	EC	22.5%
26923	Domestic	Sure-Gro IP Inc.	Wilson Antout Ant Killer Dust	DU	5%

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
27206	Domestic	Scotts Canada Ltd.	Ortho Grub-B-Gon Max Grub Eliminator Ready-To-Spray	SU	22.5%
27207	Domestic	Scotts Canada Ltd.	Ortho Bug-B-Gon Max Ant & Chinch Bug Eliminator Ready-To-Spray	SN	22.5%
27208	Domestic	Scotts Canada Ltd.	Ortho Bug-B-Gon Max Ant And Chinch Bug Eliminator Concentrate	SN	22.5%
29616	Domestic	King Home & Garden Inc.	King Bug Killer Insecticide Dust	DU	5%
29619	Domestic	King Home & Garden Inc.	King Ptv Potato, Tomato & Vegetable Dust For Bugs And Blights	DU	5%[1]
29623	Domestic	King Home & Garden Inc.	King Ant & Earwig Killer Dust	DU	5%

[1] co-formulated with other active ingredient(s), which are not listed in the table
DU = dust; EC = emulsifiable concentrate; GR = granular; SO = solid; SN = solution; SU = suspension

Reference List

Published Information

PMRA No.	Reference
1785480	Canada, 2009. Proposed Re-evaluation Decision PRVD2009-14, Carbaryl
2405939	Canada, 2013. Re-evaluation Note REV2013-06, Special Review Initiation of 23 Active Ingredients
2629416	Canada, 2016. Re-evaluation Decision RVD2016-02, Carbaryl
2304809	Request for Scientific Assessment of Carbaryl, E-mail from T. MacQuarrie to Fida'a Ali Rawabheh, Ministry of Agriculture, Jordan, 6 May 2013.
2304815	Request for Scientific Assessment of Carbaryl, E-mail from T. MacQuarrie to S. Nahawi, Ministry of State for Environment Affairs, Syrian Arab Republic, 6 May 2013.
2393042	Section 18(2) Notice of Special Review Initiation to FPT members, February 7, 2014.
2558436	European Commission, 2006. Final Review Report for the Active Substance Carbaryl, September 29, 2006, DACO: 12.5
2558433	European Commission, 2007. Commission Decision of 21 May 2007 Concerning the Non-inclusion of Carbaryl in Annex I to Council Directive 91/414/EEC and the Withdrawal of Authorisations for Plant Protection Products Containing that Substance
2652829	European Food Safety Authority 2005. Draft Assessment Report (DAR), Carbaryl, Volume 3, Annex B, B.7
1650855	European Food Safety Authority 2006. EFSA Scientific Report (2006) 80, Conclusion on the Peer Review of Carbaryl. 12 May 2006
2644467	Joint Meeting on Pesticide Residues, 1970. 1969 Evaluations of Some Pesticide Residues in Food - Carbaryl, DACO: 12.5
2652831	Rotterdam Convention 2010, PIC Circular XXXII, December 2010

Unpublished Information

PMRA No.	Reference
2431636	E-mail Response to Subsection 18(2) Notice - Special Review Initiation Notice to FPT
1195093	C. Weil et al., 1969. Carbamate, Results of Feeding in the Diets of Rats for One Week (32-57), DACO: 6.4
1183771	C. Weil, 1969. I-Naphthyl N-Hydroxymethyl Carbamate Results of Feeding in the Diets of Rats for One Week, DACO: 4.2.1
1183774	C. Weil, 1968. Results of Feeding in the Diet of Rats for One Week & for One Week Plus One Day On Control Diets (31-160), DACO: 4.2.1